PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION See Form PCT/IPEA/416	
P06262PC00		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/SE2004/000133	30.01.2004	30.01.2003
International Patent Classification (IPC) or national classification and IPC		
A61K 39/395, C07K 16/02, A61P 1/12, A61P 31/00		
Applicant		
Immun System I.M.S. AB et al		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 6 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *(sent to the applicant and to the International Bureau)* a total of 3 sheets, as follows:
      ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s))
      _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items:
   - ☒ Box No. I Basis of the report
   - ☐ Box No. II Priority
   - ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - ☐ Box No. IV Lack of unity of invention
   - ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - ☐ Box No. VI Certain documents cited
   - ☐ Box No. VII Certain defects in the international application
   - ☐ Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
13.07.2004	25.04.2005
Name and mailing address of the IPEA/SE Patent- och registreringsverket Box 5055 S-102 42 STOCKHOLM Facsimile No. +46 8 667 72 88	Authorized officer Lars Wallentin / MRo Telephone No. +46 8 782 25 00

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/SE2004/000133

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of:

☐ international search (under Rules 12.3 and 23.1(b))
☐ publication of the international application (under Rule 12.4)
☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):*

☐ the international application as originally filed/furnished

☒ the description:

pages 1-10 as originally filed/furnished
pages* _____ received by this Authority on _____
pages* _____ received by this Authority on _____

☒ the claims:

pages _____ as originally filed/furnished
pages* _____ as amended (together with any statement) under Article 19
pages* 11-13 received by this Authority on 18.02.2005
pages* _____ received by this Authority on _____

☐ the drawings:

pages _____ as originally filed/furnished
pages* _____ received by this Authority on _____
pages* _____ received by this Authority on _____

☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/figs _____
☐ the sequence listing *(specify)*: _____
☐ any table(s) related to the sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/figs _____
☐ the sequence listing *(specify)*: _____
☐ any table(s) related to the sequence listing *(specify)*: _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/SE2004/000133

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 8-19

because:

☐ the said international application, or the said claims Nos. _____
relate to the following subject matter which does not require an international preliminary examination *(specify)*:

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _____
are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 8-19

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
- ☐ has not been furnished
- ☐ does not comply with the standard

the computer readable form
- ☐ has not been furnished
- ☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in the Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/SE2004/000133

Box No. V **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	1-7	YES
	Claims		NO
Inventive step (IS)	Claims	1-7	YES
	Claims		NO
Industrial applicability (IA)	Claims	1-7	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

Reference is made to the following documents:

D1: Yoshinori Mine et al: "Chicken Egg Yolk Antibodies as Therapeutics in Enteric Infectious Disease: A Review"
D2: ZA9209143 A
D3: Kaminski M V Jr et al: Efficacy of oral anti-Candida egg yolk antibody. A Food not a drug". Journal of the American College of Nutrition 19(5), Oct 2000, abstract 55, page 688.

Note that only the abstract of ZA9209143 A (D2) was cited in the International Search Report, while the complete specification is cited in this opinion.

The claimed invention intend to provide an alternative to the use of antibiotics, antimycotics and conventional extraneous sources of bulk polyclonal mammal antibody (IgG) in treatment and prophylaxis of enteric infections in newborn infants or patients suffering from temporary immunodeficiency or immunodeficiency diseases.

D1 discusses treatment of enteric infections by oral administration of egg yolk antibodies (IgY) from immunized chickens. According to D1, such treatment may serve as an alternative to antibiotics (refer to abstract). Production and isolation of IgY from immunized chickens is discussed on page 161-162. It is noted in D1 that since the oral administration of anti-ETEC (enterotoxic E. Coli) IgY has proved to be successful for the treatment of gastrointestinal infections of animals, the clinical application of passive immunization of IgY against diarrhea is now being examined, to prevent and

.../...

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of: V

treat ETEC infection in human infants (refer to page 164, lines 36-42).

D2 discloses compositions for prophylaxis and treatment of Candida albicans infection, comprising IgY isolated from the egg yolk of domestic hens hyperimmunised with C. albicans antigen. The compositions are especially used to control recurment candiasis, without risks of inducing response which can occur during treatment with antifungal agents. The compositions may be formulated as a freeze-dried or lyophilised powder containing a buffering agent (refer to page 6, lines 18-25)

D3 discloses the use of hyperimmunized chicken´s egg yolk containing anti-Candida albicans IgY for treating candiasis in humans, as an alternative to antifungal antibodies with dangerous side effects.

None of D1-D3 specifically addresses infections in newborn infants or patients suffering from temporary immunodeficiency and immunodeficiency diseases and they do not include the Enterobacter cloacae microbe/antigen.

In D1, which is considered to be the most relevant document, no absorption of intact antibodies has been shown on humans. It is only mentioned that further studies on infants are being carried out. Newborn infants are not mentioned or suggested.

In the answer to the written opinion, the applicant states that prematurely born infants have a deficient immune system, which is also manifested in the presence of frequent Enterobacter cloacae infections. These infections strikes prematurely born infants but do not give rise to any clinical disturbances in infants or adults with normal immune system. Further, the use of antibodies for early-weaned piglets as disclosed in D1 discloses to the use of antibodies for humans when the small child is 6-12 months old. Such a child weighs 7-10 kilos and has a much more mature immune system in comparison with a newly born child.

The problem stated in the description of the invention and the solution to this problem is thus not previously known. Further, it is not considered obvious to a person skilled in the art to conclude that the known technique in D1-D3 can be altered to a use for newborn infants with use of the Enterobacter cloacae microbe/antigen. .../...

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of: V

Therefore, the claimed invention is not obvious to a person skilled in the art.

Accordingly, the invention defined in claims 1-7 is novel and is considered to involve an inventive step. The invention is also industrially applicable.

New claims

filed February 18, 2005

1. IgY that originates from an egg of a bird hyperimmunised with Enterobacter cloacae for use in prophylaxis or treatment of enteric infection in newborn infants, prematurely born infants, infants having an immature immune system, patients suffering from temporary immunodeficiency and immunodeficiency diseases such as AIDS.

2. Use according to claim 1, wherein the enteric infection is an intestinal infection.

3. Use of IgY that originates from an egg of a bird hyperimmunised with Enterobacter cloacae for the production of a pharmaceutical for treatment and/or prevention of enteric infections in newborn infants, prematurely born infants, infants having an immature immune system, patients suffering from temporary immunodeficiency and immunodeficiency diseases such as AIDS.

4. Use according to claim 3, wherein the IgY is formulated as a freeze dried or lyophilised powder, a solution, an emulsion, a lozenge, a tablet or as a capsule together with any other pharmaceutically acceptable carrier or diluent.

5. Use according to claim 4, wherein the pharmaceutical further comprises a buffering agent.

6. Use according to any of claims 4 or 5, further comprising a nutritional agent.

7. Use according to claim 5 or 6, wherein the nutritional agent or buffering agent is human breast milk or a substitute therefore.

8. Method of prophylaxis or treatment of enteric infections in newborn infants, prematurely born infants, infants having an immature immune system,

patients suffering from temporary immunodeficiency and immunodeficiency diseases such as AIDS, comprising the step of:
-administrating to said infant or patient a pharmaceutical composition comprising IgY that originates from an egg of a bird hyperimmunised with a microbe.

9. Method according to claim 11, wherein the microbe is a bacterium, virus, fungus or parasite.

10. Method according to claim 11, wherein the infection is a bacterial infection.

11. Method according to claim 11, wherein the microbe is Enterobacter cloacae.

12. Method according to claim 11, further comprising formulating the pharmaceutical composition as a freeze dried or lyophilised powder, a solution, an emulsion, a lozenge, a tablet or as a capsule or administering it together with any other pharmaceutically acceptable carrier or diluent.

13. Method according to claim 11, wherein the pharmaceutical composition is administered together with a nutritional agent.

14. Method according to claim 16, wherein the nutritional agent is human breast milk or a substitute therefore.

15. Method according to claim 11, wherein the pharmaceutical composition is administered to newborn infants having an immature immune system.

16. Method according to claim 11, wherein the pharmaceutical composition is administered to newborn infants having a weight below 2500g.

17. Method according to claim 11, wherein the pharmaceutical composition is administered to prematurely born infants.

18. Method according to claim 11, wherein the pharmaceutical composition is administered to newborn infants having a pH above 1,5 in their stomach.

19. Method according to claim 11, wherein the pharmaceutical composition is administered to newborn infants having pH between 1,5 and 4 in their stomach.